

U.S. Patent Application No. 10/524,278
Amendment dated May 13, 2008
Reply to Final Office Action of January 15, 2008

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AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in the application:

LISTING OF CLAIMS:

1. (Currently amended) An assay method for drug glucuronidation of UDP-glucuronosyltransferase 1 (UGT) (UGT1) of a subject, wherein the subject is human, comprising a step of:

detecting (a) mutation(s) in an exon 5 region of a gene coding for UGT UGT1 having a nucleotide sequence that is common to each ~~isofrom~~ isoform of UGT1A1, UGT1A3, UGT1A4, UGT1A5, UGT1A6, UGT1A7, UGT1A8, UGT1A9, and UGT1A10 for a sample including a gene coding for UGT1, without conducting an assay for each of the isoforms, that correspond(s) to nucleotide number 1456 in the genetic sequence of UGT UGT1 which encodes an amino acid at position 486 in the amino acid sequence of UGT1A1 molecule, ~~wherein detection of a mutation in an exon 5 region encoding a UGT molecule determines the enzymatic activity of the UGT molecule in drug glucuronidation; and~~

determining that, when the mutation in an exon 5 region encoding a UGT1 molecule is detected, the level of enzymatic activity of the UGT1 molecule in drug glucuronidation in the subject would be lower than that of a UGT1 molecule without the mutation;

wherein the drug glucuronidation is glucuronidation of 2-amino-5-nitro-4-trifluoromethylphenol.

2. (Original) The assay method according to claim 1, further comprising a step of detecting (a) mutation(s) of an increase or decrease in the repeating sequence of TA present in a TATA box of a promoter region.

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- 3 - 4. (Canceled)
5. (Currently amended) The assay method according to claim 1, comprising, in addition to the step of detecting the mutation(s), a step of detecting (a) mutation(s) in at least one region of the regions of exons 1, 2, 3, and 4 of a genetic sequence coding for a UGT UGT1 molecule.
6. (Currently amended) The assay method according to claim 5, comprising a step of detecting at least one genetic sequence mutation of a mutation at nucleotide number 226 in a genetic sequence of UGT UGT1 coding for an amino acid at position 71 in the amino acid sequence of UGT1A1 molecule and a mutation at nucleotide number 686 in a genetic sequence coding for an amino acid at position 229 in the amino acid sequence of UGT1A1 molecule.
7. (Withdrawn) A UGT gene having (a) mutation(s) comprising the base substitution described in claim 3, or a gene fragment including the mutation(s).
8. (Withdrawn) DNA fragments having a functionally effective length as assayed DNA that are provided for the detection method for a base substitution described in claim 1, or DNA fragments having a functionally effective length as probes for use in the detection method for a base substitution.
9. (Withdrawn) The DNA fragments according to claim 7, which are oligonucleotide probes that are specific to UGT having a base sequence set forth in any one of SEQ ID NOS: 1 to 3.

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10. (Previously presented) The assay method according to claim 5, which uses a combination of probes comprising SEQ ID NO: 1 and probes comprising SEQ ID NO: 2 and/or 3.
11. (Withdrawn) A detection device in which the oligonucleotide probes according to claim 7 are provided within the same device.
12. (Withdrawn) The detection device according to claim 11, which is a nucleic acid array or a nucleic acid chip in which an end of the base sequence of the oligonucleotide probes according to claim 7 is immobilized by bonding to an insoluble support via a functional group.
13. (Currently amended) A method for assessing, predicting or assaying drug metabolism in a human subject comprising: using a detection device in which probes comprising SEQ ID NO: 1 and probes comprising SEQ ID NO: 2 and/or 3 are provided within the same device to detect a mutation in an exon 5 region of a gene coding for UGT1 that correspond(s) to nucleotide number 1456 in the genetic sequence of UGT1 which encodes an amino acid at position 486 in the amino acid sequence of UGT1A1 molecule; and determining that, when the mutation in an exon 5 region encoding a UGT1 molecule is detected, the level of enzymatic activity of the UGT1 molecule in drug glucuronidation in the subject would be lower than that of a UGT1 molecule without the mutation; wherein the drug glucuronidation is glucuronidation of 2-amino-5-nitro-4-trifluoromethylphenol.
14. (Withdrawn) An assay kit used in an assay method for drug metabolizing activity of UDP-

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glucuronosyltransferase (UGT), comprising a step of detecting (a) mutation(s) in an exon 5 region of a gene coding for UGT, which includes the nucleic acid fragments according to claim 7.

15. (Withdrawn) An assay kit used in an assay method for drug metabolizing activity of UDP-glucuronosyltransferase (UGT), comprising a step of detecting (a) mutation(s) in an exon 5 region of a gene coding for UGT, which includes the nucleic acid fragments according to claim 8.

16. (Withdrawn) The DNA fragments according to claim 8, which are oligonucleotide probes that are specific to UGT having a base sequence set forth in any one of SEQ ID NOS: 1 to 3.

17. (Canceled)

18. (Withdrawn) A UGT gene having (a) mutation(s) comprising the base substitution described in claim 4, or a gene fragment including the mutation(s).

19. (Previously presented) The assay method according to claim 6, which uses a combination of probes comprising SEQ ID NO: 1 and probes comprising SEQ ID NO: 2 and/or 3.

20. (Currently amended) An assay method for drug glucuronidation of UDP-glucuronosyltransferase 1 (UGT) (UGT1) of a subject, wherein the subject is human, comprising: ~~a step of~~ detecting (a) mutation(s) in an exon 5 region of a gene coding for UGT

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UGT1 by using a combination of probes comprising SEQ ID NO: 1 and probes comprising SEQ ID NO: 2 and/or 3, wherein detection of a mutation in an exon 5 region encoding a UGT molecule determines the enzymatic activity of the UGT molecule in drug glucuronidation and determining that, when the mutation in an exon 5 region encoding a UGT1 molecule is detected, the level of enzymatic activity of the UGT1 molecule in drug glucuronidation in the subject would be lower than that of a UGT1 molecule without the mutation; wherein the drug glucuronidation is glucuronidation of 2-amino-5-nitro-4-trifluoromethylphenol.

21. (Previously presented) The assay method according to claim 20, further comprising a step of detecting (a) mutation(s) of an increase or decrease in the repeating sequence of TA present in a TATA box of a promoter region.

22. (Canceled).